ABSTRACT

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Title of Thesis: Design and Synthesis of Hybrid Compounds Based on Tacrine/Resveratrol Derivatives

Alzheimer‘s disease (AD) is a progressive neurodegenerative brain disorder, in which a progressive dementia appears. The cause of AD is currently unknown, however, scientific research has revealed several pathological hallmarks - β-amyloid plaques and neurofibrillary tangles. These changes cause gradual disintegration of nerve cells and they change the metabolism in the brain. The current drugs are not able to treat the cause of the disease, being able only to delay the onset of severe symptoms. The basic drugs for AD treatment are acetylcholinesterase (AChE, E.C. 3.1.1.7) inhibitors and, more recently approved, *N*-methyl-*D*-aspartate (NMDA) receptor antagonist memantine. These drugs are able to increase cholinergic activity or preventing glutamate excitotoxicity in the patient’s brain, thus improving cognitive functions and delaying severe stages of the disease. One of the emerging approaches in drug synthesis represents multi-target-directed ligands (MTDLs). Apart from the ability to inhibit AChE, they can also target more pathological processes at once. As such, they are able to bring an added value in a single molecule. In this work, we turned our attention to the preparation of hybrid compounds based on tacrine and resveratrol moieties. Tacrine scaffold act as cholinesterase inhibitor, whereas resveratrol is a strong antioxidant, naturally occurring in the vine. We assumed that coupling of these moieties could lead to the derivatives affecting multiple pathological targets of the disease and consequently represent new leads for AD therapy.